

Appl. No. : 10/646,075
Filed : August 22, 2003

REMARKS

Applicants acknowledge receipt of the Office Action mailed October 8, 2004. To summarize, the Examiner rejected Claims 32-35 and 65-68 under 35 U.S.C. §103(a) as being unpatentable over either of McCarty et al. (U.S. Patent No. 5,707,970) in view of Speck (U.S. Patent No. 6,066,659), Harrison's Principles of Internal Medicine ("Harrison's"), and Levere et al. (U.S. Patent No. 5,217,997). Additionally, Claims 32-35 and 65-68 were likewise rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 9-12 of U.S. Patent No. 5,707,970 or Claims 8-12 of U.S. Patent No. 6,156,735.

Claims 32-35 and 65-68 were pending in the application. Claims 65-68 have been canceled. Claim 32 has been amended to include an identifying step. Claim 33 has been amended to clarify that the term "disease" refers to a disease secondary to coronary vascular disease. Support for these amendments can be found throughout the specification and in the claims as originally filed. Support can be found, for example, in paragraphs [0030] and [0079] of the specification. New Claims 69-70 have been added. Support for the new claims can be found throughout the specification and in the claims as originally filed. For example, support for Claims 69 and 70 can be found in paragraphs [0079] and [0080] of the specification. The specification was likewise amended to clarify that the present application claims priority to U.S. Provisional Patent Application No. 60/405,749. No new matter has been added. Claims 32-35 and 69-70 are presented for consideration. Reconsideration and withdrawal of the present rejections in view of the comments presented herein are respectfully requested.

Claims 32-35 and 69-70 are non-obvious under 35 U.S.C. § 103(a) in view of the cited art

To articulate a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. See M.P.E.P. § 2143. If the prior art fails to meet one or more of these criteria, a *prima facie* case of obviousness cannot be asserted. Applicants submit that the contrasts between the present invention and the cited art are significant and the references are not sufficient to support a *prima facie* case of obviousness.

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The PTO infers obviousness of the present claims based upon a number of references. To summarize, the PTO asserts that the teachings of Speck, which describes atherosclerosis as a disease of the coronary vascular system, when combined with the teachings of McCarty et al., which disclose the treatment of atherosclerosis with an arginine-silicate-inositol complex, renders the present claims obvious under 35 U.S.C. §103(a). Applicants have cancelled claims 65-68 directed to a method of promoting cardiovascular health. The remaining claims (Claims 32-35 and 69-70) relate to a method of treating diseases secondary to cardiovascular disease. The PTO opines that if one were to treat a cardiovascular disease such as atherosclerosis, it would logically follow that diseases secondary to cardiovascular disease would likewise be treated. Applicants respectfully disagree and submit that none of the cited references teach, suggest, or disclose the use of an arginine-silicate-inositol complex for treating a disease secondary to coronary vascular disease. Moreover, none of the references, alone or in combination, suggest modification of the reference teachings to arrive at the presently claimed invention. Finally, the cited references provide no reasonable expectation of success in achieving the claimed invention. Accordingly, the present claims are non-obvious under 35 U.S.C. §103(a) as will be discussed in greater detail below.

There is no motivation to modify the teachings in McCarty et al., Speck, Harrison's or Levere et al. to arrive at the claimed invention

A review of the cited references makes clear that none of the references, alone or in combination, teach or suggest the claimed method of treating a disease secondary to cardiovascular disease nor do they provide a motivation to modify the reference teachings to arrive at the claimed invention. McCarty et al. is directed to compositions comprising arginine-silicate-inositol for the treatment of atherosclerosis or for arginine supplementation. As suggested above, Speck teaches that atherosclerosis is a primary disease of the coronary vascular system. However, both McCarty and Speck are silent with respect to any advantages arginine-silicate-inositol complexes might have in treating diseases secondary to coronary vascular disease as is presently claimed. The PTO cite to Harrison's, which teaches that nephrosclerosis can be treated by controlling hypertension as further support for finding the present claims obvious. Again, Harrison's does not describe or recognize the role that arginine-silicate-inositol plays in promoting cardiovascular health. Finally, Levere et al. is cited as teaching that the administration of arginine reduces hypertension. Thus, according to the PTO, a skilled artisan would be

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motivated to administer an arginine silicate inositol complex as taught in McCarty as a source of arginine supplementation with the teachings of Harrison's to reduce hypertension and, by extension, treat nephrosclerosis.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Kotzab, 217 F.3d 1365 (Fed. Cir. 2000). Applicants submit that the Examiner has pointed to no motivation to modify the reference teachings to arrive at the claimed method of treating diseases secondary to cardiovascular disease. All of the references are completely silent as to any benefits the administration of arginine-silicate-inositol complex might evince in ameliorating the symptoms or underlying diseases secondary to coronary vascular disease. Moreover, none of the cited references describe, suggest, or appreciate the role of arginine-silicate-inositol in treating diseases secondary to coronary vascular disease. A skilled artisan, therefore, would have no motivation, based upon the teachings of the cited references, to administer arginine-silicate-inositol to treat, for example, nephrosclerosis, microvascular complications, macrovascular complications, and abnormal lipid profiles as is presently claimed.

The mere fact that the reference teachings might be modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. See In re Mills, 16 U.S.P.Q.2d 1430 (Fed Cir. 1990); See, also M.P.E.P. §2143.01. The McCarty reference is silent with respect to the advantages of arginine-silicate-inositol administration for treating any secondary diseases associated with cardiovascular disease but focuses instead on the treatment of a primary cardiovascular disease, namely atherosclerosis. The remaining references fail to recognize any relationship between an arginine-silicate-inositol complex and the treatment of diseases secondary to cardiovascular disease. In In re Fine, the Federal Circuit made clear that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Instead, there must be some reason, suggestion, or motivation found in the cited references whereby a person of ordinary skill in the art would make the combination and that knowledge cannot come from the applicant's disclosed invention. See In re Oetiker, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992).

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Absent impermissible hindsight, it would not have been obvious to administer an arginine-silicate-inositol complex such as the complex described in McCarty et al. to treat, for example, nephrosclerosis, macro- and/or micro-vascular complications, and abnormal lipid concentrations. Accordingly, Claims 32-35 and 69-70 are not obvious in view of the cited references.

There is no reasonable expectation of success in achieving the claimed invention by modifying the reference teachings

Furthermore, a *prima facie* case for obviousness is established only when the PTO provides references that would lead one of ordinary skill in the art to believe that he or she would have a reasonable expectation of success in practicing the claimed invention in view of the cited art. See *In re Merck & Co., Inc.*, 231 U.S.P.Q. 375 (Fed. Cir. 1986); M.P.E.P. § 2143.02. Applicants respectfully submit that there is no reasonable expectation of success in achieving the claimed invention by modifying the teachings of the cited art. The level of unpredictability in the art is high as the present invention relates to the effects of a multi-component complex on a biological system. The level of unpredictability increases geometrically as additional ingredients are combined to achieve a certain effect. The present invention is directed to a complex comprising at least three components: arginine, silicate, and inositol. Each of these components has biological activity which can contribute to the complex's effect on coronary vascular disease and/or diseases secondary to coronary vascular disease. As detailed in the specification at, for example, paragraph [0040], both arginine and silicate can exert separate anti-atherosclerotic effects. The level of unpredictability increases geometrically as additional ingredients are combined to achieve a certain effect.

Levere et al. describe the administration of arginine alone for treating hypertension. The PTO presupposes that arginine-silicate-inositol would work in the same fashion as arginine alone to treat diseases quite distinct from hypertension. Arginine and an arginine-silicate-inositol complex are different compounds with different chemical structures, molecular weights, and biological activity. Moreover, hypertension is a disease entirely separate from the presently claimed diseases secondary to coronary vascular disease such as nephrosclerosis, macro and micro vascular complications, and abnormal lipid concentrations. There is no suggestion, motivation, or expectation of success set forth in the cited references that a treatment for hypertension would work equally well for unrelated, distinct diseases which are secondary to

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coronary vascular disease. Given the unpredictability in the art and the lack of guidance provided by the cited references, a skilled artisan would not expect that arginine, as taught in Levere et al., could be substituted with a multi-component complex to achieve a method of treating diseases separate and distinct from any disease taught in the prior art. Accordingly, the rejection of Claims 32-35 as obvious under 35 U.S.C. §103(a) should be withdrawn.

The prior art does not teach each and every limitation of the claims

Finally, in order to establish a case for obviousness, the Examiner must cite prior art that teaches or suggests all the claim limitations. See M.P.E.P. § 2143.03. Independent Claim 32 has been amended to recite a method of treating a disease secondary to coronary vascular disease comprising identifying an individual suffering from a disease secondary to coronary vascular disease and administering an effective amount of an arginine silicate inositol complex to treat the disease. Applicants respectfully submit that none of the cited references, alone or in combination, teach the step of identifying an individual suffering from a disease secondary to coronary vascular disease. Because the cited references fail to teach or suggest all of the limitations of the claims, the rejection of the claims as obvious should be withdrawn.

Regarding the Double Patenting Rejection

Claims 32-35 and 65-68 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-12 of U.S. Patent No. 5,707,970 (the '970 patent) or Claims 8-12 of U.S. Patent No. 6,156,735 (the '735 patent) in view of Speck (U.S. Patent No. 6,066,659), Harrison's Principles of Internal Medicine ("Harrison's") and Levere et al. (U.S. Patent No. 5,217,997). A terminal disclaimer is submitted herewith, thereby obviating the objection to Claims 32-35 and 65-68 in view of the '970 and '735 patents. Applicants have already distinguished the remaining references from the claimed invention in their response to the §103(a) rejection. Accordingly, withdrawal of the rejection of Claims 32-35 and 65-68 under the judicially created doctrine of obviousness-type double patenting is earnestly solicited.

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CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the present application is in condition for allowance. Nevertheless, the PTO is invited to contact the undersigned at the telephone number appearing below to discuss any remaining issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 1/7/05

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